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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,023	06/28/2001	Vladmir R. Muzukantov	PENN-0749	7329

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EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/08/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/762,023

Applicant(s)
Muzukantov et al.

Examiner
Marianne DiBrino

Art Unit
1644



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-8 are subject to restriction and/or election requirements.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. **Please Note:** In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-4, drawn to a method for targeting and prolonging association of a selected drug to the luminal surface of pulmonary vascular endothelium (pev) comprising administering an drug and a non-internalizable antibody against an antigen on the luminal surface of the pev.

II. Claims 5-8, drawn to a method for dissolution of fibrin clots or prevention of intravascular coagulation in the pulmonary vasculature comprising administering a fibrinolytic or anticoagulant in combination with a non-internalizable antibody against an antigen on the luminal surface of the pev.

3. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claim 1 of the instant application does not provide a technical feature that is distinguished over the prior art, as evidenced by Bowes et al (1995, IDS reference) in view of Imaizumi (IDS Reference) and further in view of Mulligan et al (IDS Reference) and Panes et al (IDS Reference). Bowes et al teach that administration of an anti-ICAM-1 mAb and the drug tPA to rabbits prevents leukocyte adhesion and increases post ischemic duration at which thrombolytic therapy remains effective in cerebral ischemia and reperfusion (especially Abstract). Bowes et al further teach that administration of tPA alone improves neurologic outcome in models of ischemia, but that obstacles exist to therapy, and further that reperfusion may also result in additional neurologic damage as ischemic tissue is reoxygenated. Bowes et al do not teach a method for targeting and prolonging association of a selected drug to the

luminal surface of the pulmonary vascular endothelium comprising administering to an animal a selected drug in combination with a non-internalizable antibody which binds to the luminal surface of the endothelium. Imaizumi teaches a method of administration of mouse anti-rat mAb 1A29 (anti-ICAM-1) inhibits ICAM-1 on pulmonary vascular endothelial cells and impairs damage due to reperfusion injury. Imaizumi teaches that impairment of reperfusion injury is closely associated with vascular endothelial cell damage by neutrophils. Imaizumi further teaches that in flowing blood, neutrophils do not adhere to vascular endothelial cells in the normal state; adhesion of neutrophils to vascular endothelial cells is necessary to induce vascular endothelial cell damage after ischemia and reperfusion, and an increase in the expression of adhesion molecule (especially page 2852, column 1). Imaizumi teaches an increase in the expression of adhesion molecules in vascular endothelial cells activated by reperfusion and a resultant increase in the binding to neutrophils. Mulligan et al teach anti-ICAM-1 mAb 1A29 accumulates in the pulmonary vasculature, i.e., binds to the luminal surface of the endothelium and is not internalized, challenged with pro-inflammatory agents, and that blocking of ICAM-1 is tissue protective in a manner in which neutrophil recruitment is attenuated. Panes et al teach that ICAM-1 is constitutively expressed on vascular endothelium of the rat and there are significant regional differences in magnitude of expression. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted the mAb 1A29 of Imaizumi or of Mulligan et al for the anti-ICAM-1 mAb in the composition of Bowes et al and to have used the combined composition in the method of Imaizumi and given the teaching of Panes et al that ICAM-1 is constitutively expressed on vascular endothelium. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat ischemia and pulmonary reperfusion injury in rats.

Therefore, because the said claim does not provide a special technical feature, the instant invention lacks an inventive step and therefore lacks Unity of Invention.

4. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.



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Technology Center 1600
September 30, 2002



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